DEVELOPMENT OF MICROBIAL RISK ASSESSMENT METHODS

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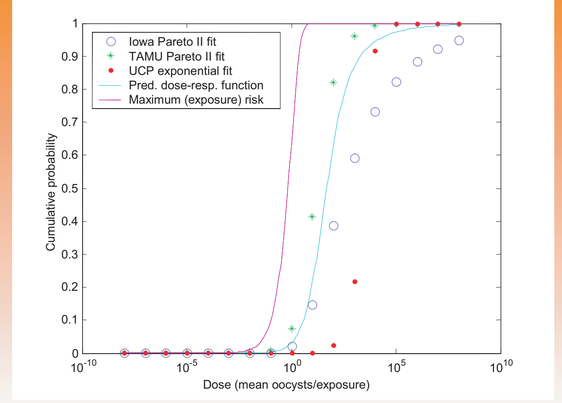
What risk assessment methods are needed to estimate dose-response, individual risk, population risk, and transmission rates?

How can risks of exposure, infection, and illness be estimated for the general population versus specific subpopulations when susceptibility, infection rate, and disease outcome differences are unknown?

The methods development program addresses three major microbial risk assessment (MRA) issues:

METHODS/APPROACH

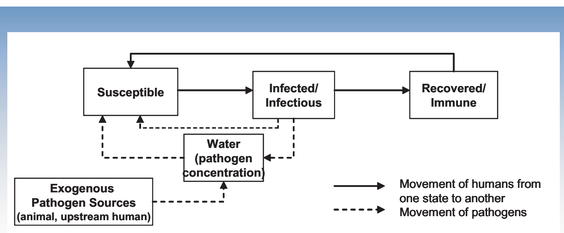
Research and development of predictive dose-response models particularly for low dose extrapolation with limited data including Bayesian approaches: ORD scientists are working with University of Miami collaborators to develop predictive Bayesian dose-response models for estimates of risk represented by the low-dose exposure range found in source, recreational and drinking water. Unlike traditional "confidence interval" approaches, the predictive Bayesian approach generates a single risk curve– which can be interpreted as a "believed" risk– that is more conservative (protective) when data are sparse.



RESULTS/CONCLUSIONS

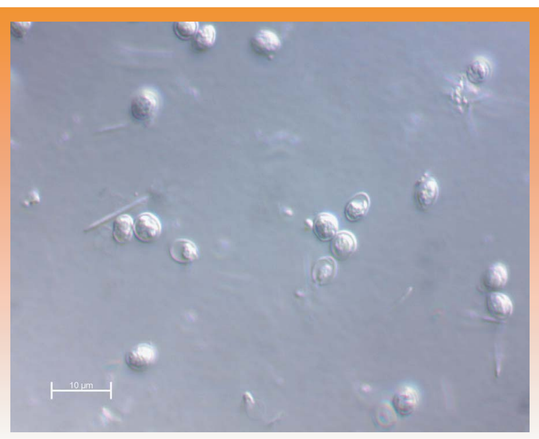
The figure shows the results of the model applied to three Cryptosporidium strains of widely varying infectivity. The log of the cumulative fraction of the population responding is plotted against the log of dose to show the response in the environmentally-relevant low-dose range. The dashed red line shows the maximum possible risk for 100% infectivity. The predictive Bayesian risk curve lies much closer to the response for the most infective strain than the least, reflecting the fairly sparse nature of the data. Should more Cryptosporidium dose-response data become available, the risk curve should shift to the right, predicting lower risk. With the current data set, the predictive Bayesian risk is about twice that of more traditional models.

Research and development of dynamic systems models to investigate risks associated with primary and secondary disease transmission at the population systems level. Cooperative agreements with two universities have resulted in the development of differential equation and stochastic models for evaluation of the various possible routes of transmission of a waterborne pathogen (e.g., water-person, person-to-person, person-to-water-to-person). This systems perspective provides a biologically-based approach to modeling population risks; in particular, this modeling framework allows for the explicit consideration of the effects of multiple interdependent transmission pathways.



The dynamic systems research provides the Agency with an awareness of the importance of considering indirect, population-level effects (such as secondary transmission and immunity) on total risk. The particular transmission models developed will be valuable for evaluating specific problem scenarios such as the expected health effects associated with risk management interventions (e.g., point-of-use tap water filter systems compared to central treatment plant controls). The researchers also demonstrated methods to derive transmission parameter values from endemic as well as outbreak data.

Development and integration of information on susceptibility and disease rates in healthy versus compromised populations. ORD scientists are working with FDA's, National Center for Toxicological Research (NCTR) in ongoing experimental animal research with the protozoan *Cryptosporidium parvum* to quantify primary and secondary transmission rates, dose-response, disease course and outcomes in animal subgroups representing healthy and compromised human population groups.



Cryptosporidium images provided by Alan Lindquist/US EPA

The animal feeding studies are currently in progress at the NCTR laboratories. There are animal groups in this study designed to represent elderly, pregnant, and malnourished subpopulations. The intent is to identify any differences in infection rate, illness rate, and severity of outcome between these groups and healthy control groups. Additional studies are designed to investigate secondary transmission issues.

RESEARCH GOALS

Through numerous collaborations with other Federal agencies, academia, and other EPA scientists, ORD scientists are working to develop microbial risk assessment methods, building upon existing guidelines and frameworks. ORD scientists are now looking at methods to handle pathogen infection and disease as well as intoxication risk by microbial biotoxins. The goals of methods development are to address uncertainties in dose-response modeling, use epidemiological or clinical information, determine human populations susceptibility differences, evaluate multiple source pathogen exposures, analyze primary and secondary transmission, and determine variable pathogen virulence and virulence factors.

FUTURE DIRECTIONS

The use of new methods will overcome data gaps, improve the design of future experiments, and drive selective research to define sensitive populations, transmission rates between people, transmission systems, and relative source contribution. Additional research is planned in secondary transmission model application and assessment of the impact of waterborne outbreaks on sensitive populations, as well as the role those populations may play in transmission.

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